Balancing benefits and harms in public health prevention programmes mandated by governments

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Even when scientific evidence for a preventive health intervention is strong, many barriers exist to population-wide implementation

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The principal rationale for medical research is to improve health. In clinical medicine, the goal is to get the results of medical research to individual patients as soon as possible. In preventive medicine, however, the challenge is to apply clinical and epidemiological evidence to whole populations. The most effective way to do this is through government legislation. However, once a government requires an intervention, individuals may have little chance to influence whether they are exposed to it. This means that government decisions to require prevention measures are political. Unless the decision is anchored securely in science, even weak political arguments can over-rule the science and the needs of public health. We consider the challenges that face the introduction and maintenance of evidence based public health interventions using the current debates over preventing birth defects by fortification of flour with folic acid and the safety of the MMR (measles, mumps, and rubella) vaccine.[1 2]

Fortification of cereal grains with folic acid

Two randomised controlled trials and data from controlled observational studies provide a strong scientific basis for the consensus that synthetic folic acid can prevent spina bifida and anencephaly.[3 4] The main ways to get synthetic folic acid are from fortified food or vitamin pills. Some countries have chosen to rely on vitamin pills and others have fortified flour and other cereal grain products.

The United Kingdom and Netherlands have attempted to protect the population fully through health education programmes. In both countries, most people do not consume vitamin pills. The education programmes have increased the number of pregnant women who take folic acid pills before pregnancy to about 50%, but they provide no protection for the 50% who do not take folic acid.[5 6] Dependence on individual behaviour has thus failed in half of pregnancies. These results suggest that maximising the prevention of birth defects requires fortification of centrally produced and widely eaten food.

The United States is one of more than 30 countries that have required mandatory fortification with folic acid. Since 1942, the Food and Drug Administration has required "enriched" cereal grains to contain certain vitamins and minerals, the logic being that producing white flour removed vitamins that should be restored. Folic acid was not originally included, but the 1992 US Public Health Service folic acid recommendations suggested fortification. In March 1996, the Food and Drug Administration issued regulations requiring that enriched grains be fortified by 1 January 1998 but at a level that would have the median woman consume only a quarter of the recommended amount of folic acid.[7] Fortification has resulted in about a 25% reduction in spina bifida and anencephaly and in elimination of folate deficiency anaemia.[8 9] In addition, analysis of recent national mortality data suggest that fortification prevented 50 times more deaths from stroke and heart attack than cases of birth defects each year.[10]

Despite the documented success of mandatory fortification, New Zealand, Australia, the United Kingdom, and other European countries have not required fortification. We discuss below arguments that limited the fortification concentration in the United States because they still impede mandatory fortification elsewhere.

Safety

A government proposal to require the population to be exposed to an intervention should prompt a complete and careful scientific review of safety data. Since you cannot prove a negative, opponents to the intervention can always hypothesise some unidentified risk that would be recognised only after the intervention is implemented.

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Fortification with folic acid has important public health benefits

In the 1950s, investigators showed that high doses of folic acid (5000 to 50 000 µg a day) were not effective treatment for the neuropathy of pernicious anaemia but could often cure the anaemia. These observations led to the hypothesis that consumption of folic acid by people with undiagnosed pernicious anaemia (and other causes of severe vitamin B12 deficiency) might delay the diagnosis and treatment. This concept, often referred to as masking, is the primary safety issue related to folic acid fortification. Policy discussions were framed as, "Yes, fortification will be good for babies but it may hurt their grandparents." A committee of the Institute of Medicine therefore reviewed the literature and concluded that if any risk existed, it began at 5000 µg or more a day.[11]

Unwillingness to consider all possible evidence of benefit

For reasons that are not clear, policy discussions over the past decade have dismissed the idea that fortification of flour with folic acid could be of benefit to anyone other than developing embryos.[12] Homocysteine is accepted to be an important independent risk factor for occlusive cardiovascular disease, and consumption of folic acid has been shown to lower serum homocysteine concentrations. Controlled observational studies show that consuming folic acid protects against cardiovascular disease.[13]

Although observational studies have repeatedly provided the basis of public health policy—from antismoking campaigns to prevention of obesity—they have been dismissed as insufficient to show benefit in discussions of folic acid fortification. Policy reviews have been willing to consider data only from randomised controlled trials, and they have not referenced an existing trial showing substantial protection.[12 14] No review has balanced the risk of folic acid fortification for the general population against the benefit from reduction of cardiovascular disease. Hence policy makers do not have a balanced view of the risks and benefits.

Choice

Discussions of mandatory fortification often raise the issue of choice. If all flour is fortified, people will be forced to eat fortified products even if they do not want to. Here is the classic dilemma of population protection versus individual rights. The regulatory process in the United States has a built-in solution that minimises this issue. Whole grain flours are not enriched and offer a good alternative. Given that most people in the United States eat enriched grain products, there is near universal consumption of products fortified with folic acid. Another method of maintaining choice would be to have specially labelled unfortified bread and grain products. The issue of choice remains an obstacle to mandatory fortification in the United Kingdom and New Zealand despite the availability of relatively simple solutions.

Government permission for voluntary fortification

A government can permit an intervention without requiring it. Such a position could solve the choice issue, but this strategy has not proved effective for fortification. In the United Kingdom, New Zealand, and Australia, millers are allowed to fortify grains. However, millers and bakers have been slow to make and sell enriched products. In the United States, folic acid fortification was not permitted until 1996, when the regulations were issued for mandatory fortification of enriched cereal grains 21 months later. As it turned out, knowing that universal fortification would be required by 1 January 1998, most millers fortified their products voluntarily before the mandatory deadline. Widespread voluntary fortification seems unlikely unless regulations requiring mandatory fortification are viewed as inevitable.

Custom, tradition, and dogma

Scientific disciplines may hold to traditions that resist population-wide, mandatory prevention programmes. The food and nutrition community customarily resists the medicalisation of the food supply through fortification. It holds that any nutritional need can be obtained from simply eating the right amount of the proper foods and that natural is better than synthetic. Although the traditional position often serves the population well, this is not always the case. Food policy, like medical research, exists to improve health. Public health policy should be based on a thorough and critical review of the scientific evidence by open minds unfettered by custom and dogma.

Inertia

Implementing a population-wide, mandatory prevention programme requires changing the status quo. Inertia has to be overcome. When the inertia leads to complacency, the public may not be served well. Often policy decisions regarding public health interventions will have to be made without all the desirable data. Policy making requires a judgment, and there is some probability that the judgment may prove to be wrong. This makes continuous monitoring of safety essential, as the recent MMR vaccine controversy illustrates well.

Lessons from vaccines

Serious childhood infections that can be prevented through vaccinations now occur so rarely in industrialised countries that most of today's parents have little understanding of their threat. In contrast, worry about safety of vaccines is so widespread that some children are not vaccinated. Unvaccinated children carry a proved risk of disease and serve as a potential source of disease outbreaks. The challenge today is not efficacy of vaccines but, rather, safety. The governmental agencies responsible for immunisation programmes must work to assure safety, or this great public health achievement of the 20th century will be eroded.

In the case of the MMR vaccine, a single paper in a reputable journal raised the spectre that the vaccine caused autism while presenting no data to support this proposal. Ten of the 12 authors have now repudiated the suggested link with autism. In the intervening four years, however, many children have not been vaccinated, lawsuits have been filed, and energy, emotion, and money have been diverted from efforts to understand the basis of autism and how to manage it.

The concern for vaccine safety is not new. An Anti-vaccination Society arose in England within a few years of Jenner's first inoculations, and in the 1980s, questions about the safety of vaccines, particularly for whooping cough, led to a major rebellion against immunisations. Lawsuits alleging damage by vaccines

increased, and many vaccine manufacturers shut down production. In response, the US Congress passed legislation that included a mandate to the Institute of Medicine to determine by scientific review whether childhood vaccines can cause any of a broad array of adverse events. The institute's conclusions have been used to guide a compensation process, litigation, and public education and pointed to needed research.[2]

The best way to monitor the safety of population-wide interventions required by governments should be considered during the initial decision making. When serious safety concerns arise, as with the MMR and pertussis vaccines, governments have to investigate vigorously the proposed causal relationship. The analysis must be based on review of existing scientific data, and if these data are inconclusive, on new research. The United States has given responsibility for such analysis to the Institute of Medicine, which uses multidisciplinary committees of experts selected for their objectivity and freedom from conflict of interest. Whatever body is used to rule on safety, its conclusions must be the result of critical, open minded analysis based on science and reason.

Conclusions

Effective preventive medicine often requires population based measures that limit individual choice. Research will undoubtedly produce more examples in which prevention can best be achieved by government action. Policy makers should start with an unbiased, reasoned analysis of the best available scientific evidence, then consider the practical realities of cost, public acceptance, and political risk. The policy decision may prove a difficult, discomforting challenge. The rewards, however, could be substantial, as shown by the great public health successes of the past.

Contributors and sources: GPO is a paediatric epidemiologist who was director of the division of birth defects and developmental disabilities at the Centers for Disease Control when the MRC study was published proving that oral synthetic folic acid would prevent most of the cases spina bifida. GPO and his group provided the scientific rationale and the policy guidance and energy that led to mandatory fortification of "enriched" grains with folic acid in the United States. As medical director of the March of Dimes Birth Defects Foundation, FBJ gathered for the US Food and Drug Administration the judgments of the professional medical organisations regarding the benefits and risks of folic acid fortification of grain products. He has chaired or served on a series of US Institute of Medicine committees that have assessed causal relations between vaccines and various putative adverse events, including autism.

Summary points

The most effective way to get preventive interventions to the whole population is through government legislation

Such legislation inevitably restricts personal choice

Decisions to legislate should be based on an unbiased analysis of scientific evidence

Governments have a responsibility to monitor safety and carefully investigate any concerns that arise

Competing interests: GPO is a co-inventor on a patent that would cover putting folic acid in oral contraceptives. If there is income, it will be under the rules of the Centres for Disease Control, where he worked at the time of the invention. GPO is a paid consultant to Johnson and Johnson on this issue.

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Commentary: silent prevention

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Oakley and Johnston correctly criticise Britain's failure to fortify flour with folic acid. But the interventionist principle in nutrition and other areas of public health goes beyond folate. Contrary to current perception, the key to effective public health is not individual choice but collective action linked to public trust in its value.

Most of the main determinants of health vary little among people in a community. The scope for individuals to choose healthy and safe foods, drinks, transport, or buildings is limited; the similarities in exposure are greater than the potential differences. To differ significantly from the collective norm we would have to isolate ourselves from the mainstream of society. It is glib and disingenuous to say that we are all consumers exercising choices, when most of the options are essentially similar. For example, most

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